

Educational Effects Using a Robot Patient Simulation System for Development of Clinical Attitude

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Abstract

Introduction: The aim of this study was to assess the effectiveness of improving the attitude of dental students toward the use of a full-body patient simulation system (SIMROID) compared to the traditional mannequin (CLINSIM) for dental clinical education.

Materials and methods: The participants were 10 male undergraduate dental students who had finished clinical training in the university hospital 1 year before this study started. They performed a crown preparation on an upper premolar tooth using SIMROID and CLINSIM as the practical clinical trials. The elapsed time for preparation was recorded. The taper of the abutment teeth was measured using a 3-dimensional shape-measuring device after this trial. In addition, a self-reported questionnaire was collected that included physical pain, treatment safety, and maintaining a clean area for each simulator. Qualitative data analysis of a free format report about SIMROID was performed using text-mining analysis. This trial was performed twice at 1-month intervals.

Results: The students considered physical pain, treatment safety, and a clean area for SIMROID significantly better than that for CLINSIM ($P < 0.01$). The elapsed time of preparation in the second practical clinical trial was significantly lower than in the first for SIMROID and CLINSIM ($P < 0.01$). However, there were no significant differences between the abutment tapers for both systems. For the text-mining analysis, most of the students wrote that SIMROID was similar to real patients.

Conclusion: The use of SIMROID was proven to be effective in improving the attitude of students toward patients, thereby giving importance to considerations for actual patients during dental treatment.

1

2 **Introduction**

3 In 2006, the Ministry of Health, Labor, and Welfare (MHLW) in Japan released an
4 annual report to promote a comprehensive medical care program from the patients'
5 perspective, to establish a medical cooperation system for providing high-quality and
6 appropriate medical care, and to secure and develop good medical professionals. It also
7 proposed to improve medical quality and safety in 2015. Furthermore, the Ministry of
8 Education, Culture, Sports, Science, and Technology (MEXT) in Japan proposed to
9 improve the educational quality of the dental educational system and to evaluate the
10 clinical skills and attitudes of dental students after clinical training. To provide safe and
11 quality dental treatment, dental students have to develop basic attitudes, knowledge, and
12 skills for patients.

13 Dentists usually do many invasive treatments for patients such as tooth
14 restorations, pulp extirpation, or tooth extraction. It is therefore important that dental
15 students have enough opportunities to practice dental treatment using jaw models and
16 traditional mannequins before clinical training.¹ Furthermore, it is necessary to acquire
17 adequate clinical skills through frequent practice using these training materials before
18 treating actual patients.² Regrettably, training using jaw models focuses only on the
19 acquisition of dental technical skills and not on the patient's interest. Educating
20 undergraduate dental students includes communication, management, and the
21 consideration of patients through practical clinical training. However, patients' thoughts
22 about dental treatment have changed in recent years. Patients need more reliable
23 treatment from university hospitals. Consequently, the numbers of patients who allow
24 treatment by undergraduate dental students have significantly decreased. Therefore, the

1 dental education simulation system using a robot patient was developed to improve
2 treatment skills and communication with patients.³ The robot patient, designed as a
3 full-body human model, is equipped with the ability to perform various movements and
4 can provide training in communication and treatment skills.

5 In a previous study using a robot patient, dental students and dental trainees
6 performed prosthodontic training.⁴ All participants recognized the efficiency of this
7 system because their clinical skills increased for irreversible and invasive dental
8 treatments. This system had the possibility of improving dental treatment skills and
9 management for undergraduate and postgraduate future dental education.⁴ This previous
10 study evaluated the results of the questionnaire only after practice and did not compare
11 it to other simulators such as traditional mannequins. Thus, the first aim of this study
12 was to prove that a robot patient system is an effective simulator for clinical skill
13 education compared to another simulator that does not have facial expression and
14 movements for clinical skill education including the students' attitude. Furthermore, the
15 second aim was to verify whether this system could evaluate treatment skills compared
16 to the jaw model or traditional mannequins. A null hypothesis was then designed that a
17 robot patient system had an equal performance with the traditional mannequin without
18 attitude and movements.

20 **Material and methods**

21 *1. Subjects and examination period*

22 Ten male undergraduate dental students (23 to 24 years old) who finished their clinical
23 training at our hospital in 2014 were recruited as participants in this study. The
24 examination period was performed just after the end of their annual clinical training and

the examination time was between 5:00 PM and 8:00 PM. Each participant performed basic dental treatments such as taking impressions, filling tooth decay, being in charge of a certain patient, and communicating sufficiently with their patient during their clinical training, except during irreversible and invasive dental treatments. The study protocol was approved by the Research Ethics Committee of Tokushima University Hospital (No. 2224) and written informed consent was collected.

2. Simulation system

Two different dental simulation systems were used in this study, the full-body robot patient simulation system (SIMROID; Morita Co., Tokyo, Japan) (Figures 1-1 and 1-2), and the traditional dental training system, a half-body mannequin (CLINSIM; Morita Co., Tokyo, Japan) (Figure 2).

The SIMROID is a robot-based interactive patient stimulation system for dental training. It consists of a humanoid robot patient with a realistic appearance and reactions such as expression, movement, and speech. It also reacts to pressure on the body as physical pain. The system includes a dental chair with a full-body robot patient, a dental unit, a graphical user interface (GUI) software running on Windows XP, and 2 CCD videos to record the attitude and skills due to feedback.² The instructor operates the GUI software to act as an intermediary between the students and the robot patient while considering a natural scenario (Figures 1-1 and 1-2).

On the other hand, CLINSIM is a set of phantom models simulating the upper half of the body in a dental chair and an articulator to reproduce jaw movements. This practical dental chair is equipped with a shadowless lamp, high- and low-speed handpiece, vacuum and 3-way syringe, and the ability to be moved freely as with a real

dental chair in the clinic.

3. Experiment objects and design

A plastic upper left first pre-molar was used for the abutment preparation to fabricate a full crown. The time was measured until each student was fully satisfied. If the robot patient rinsed out during practice, the measurement time was briefly discontinued. An assistant supported each student during abutment preparation, such as handling the vacuum or adjusting the shadowless lamp (Figures 3-1 and 3-2).

The students were assigned randomly to 2 groups. Group A performed CLINSIM and SIMROID, in that order, as the first practical clinical trial, and took a break for half an hour between each practice. One month later, the same group performed in the reverse order with that of the previous examination, which is SIMRIOD and CLINSIM, as the second practical clinical trial. Group B did the opposite trial against Group A (Figure 4). After the practical clinical trials using the 2 types of simulators, the subjects answered 7 questions with a 4-level scale, where 1 means very low and 4 means very high, and wrote a free description about SIMROID (Table 1).

The model of the abutment tooth was taken from the jaw and the 4 tapers of the model were evaluated using a 3-dimensional shape-measuring device (SURFLACER VMS-100XR, UNISN Co. Osaka, Japan; Figure 5-1). The measurement tapers were the mesio-distal plane, the bucco-palatal plane, the mesio-bucco-disto-palatal corner, and the disto bucco-mesio palatal corner (Figure 5-2).

4. Statistical analysis

1 The questionnaire data with the 4-grade scale, which had 7 questions, were compared
2 between the first and second practical clinical trials for each system using Wilcoxon's
3 signed- rank test and between SIMROID and CLINSIM for each examination using the
4 Mann-Whitney U test.

5 Data, which included preparation time and taper, were tested for normality of
6 distribution using the Shapiro-Wilk test and compared between the first and second
7 practical clinical trials or between SIMROID and CLINSIM. Repeated measures
8 analysis of variance (rANOVA) were performed with the practical clinical trial (first
9 and second practical clinical trial) as a repeated measure and system (SIMROID,
10 CLINSIM) as the between-group factor for the preparation time or taper. Paired t-tests
11 or 2-sample t-tests were performed for normal distribution, but Wilcoxon's signed-rank
12 test or the Mann-Whitney U test were performed for non-normal distribution. All
13 statistical calculations were performed using SPSS (Version 22.0, IBM Corp., Chicago,
14 IL, USA). A P value < 0.05 was used for statistical significance.

15 Text data analysis for the report described in a free format was performed with
16 SPSS Text Analytics for Surveys (Version 4.0.1, IBM Corp., Chicago, IL, USA). Text
17 data mining derived the high-quality and high-frequency information through the report
18 and estimates of the students' motive. Sensitivity analysis was then performed as
19 sensitivity category, and high-frequency words were picked up through the report (Q8).
20 The sensitivity analysis judged whether sentences from the document that the subjects
21 wrote were positive or negative. The multiplicity and correspondence relationship
22 between the sensitivity category and the high-frequency words were drawn as the
23 correlation diagram and could show each connection in this present study.

Results

1. *Feelings about SIMROID*

Although a significant difference was not seen between the first and second practical clinical trial, the subjects answered that the oral cavity of SIMROID was slightly similar to an actual patient in Q1 (Figure 6). The answer about the level of difficulty to perform the abutment preparation using SIMROID against CLINSIM was significantly higher in the second practical clinical trial than in the first in Q2 ($P = 0.02$, Figure 7). The subjects felt that it was “somewhat difficult” or “very difficult” to perform the abutment preparation in the first practical clinical trial, but most of the students felt that it was “very difficult” in the second practical clinical trial of the answer for this question. Furthermore, for the motivation to retry the practice using each system in Q3, the subjects had significantly lower motivation in the second practical clinical trial than in the first using SIMROID ($P = 0.04$, Figure 8-1). However, there was no significant difference between the first and second practical clinical trial using CLINSIM.

2. *Consideration of physical pain, treatment safety, and clean area in SIMROID and CLINSIM*

For consideration of physical pain for the patients in Q4, treatment safety for the patients in Q5, and the clean area during practice in Q6, the results of the comparison between SIMROID and CLINSIM in each examination denoted the same tendency. Thus, consideration for the patients had significantly higher scores using SIMROID than using CLINSIM (each $P < 0.01$, Figures 8-2, 8-3, and 8-4). They were especially

careful not to cause physical pain during examination by paying attention not to touch the body of the robot (SIMROID) compared to that of the mannequin (CLINSIM). However, there were no significant changes through the first and second practical clinical trials for each simulation.

3. Evaluation of the abutment preparation

Self-evaluations of the abutment preparation in Q7 were not significantly different between each practical clinical trial or each system (Figure 8-5). For an objective analysis of the abutment preparation, the second practical clinical trial significantly reduced the preparation time when compared to the first practical clinical trial for SIMROID and CLINSIM ($P < 0.01$, respectively, Table 2). However, there were no significant differences between SIMROID and CLINSIM for each examination. Moreover, 4 parts of the taper preparation in the abutment tooth were evaluated. There were no significant interactions between the practice and the system. Although the bucco-palatal taper in the second practical clinical trial for CLINSIM had a smaller angle than in the first practical clinical trial ($P = 0.02$, Table 2), other tapers were not significantly different between the first and second practical clinical trials for each system. Furthermore, there were no significant differences between SIMROID and CLINSIM for each examination.

4. The report described in a free format about SIMROID

The free format survey about the expression of SIMROID in Q8 was performed after each practical clinical trial. For sensitivity analysis, 5 subjects expressed positive

opinions, 3 subjects expressed negative opinions, and 2 opinions did not belong to the positive and negative category in the first practical clinical trial. Additionally, 5 subjects expressed positive opinions, 2 subjects expressed negative opinions, and 3 opinions did not belong to the positive and negative category in the second practical clinical trial. We focused on the common words to pick up important contents from the reports in each practical clinical trial. The common words of “patient,” “practice,” “actual,” and “mannequin” were picked up through the reports of the first and second practical clinical trials (Figure 9).

Discussion

Dentists have to take responsibility for public oral health maintenance and promotion and the expectation for dental treatment is gradually becoming high. Furthermore, because patients are interested in the quality of oral health and the decline in dental clinical ability is recognized year after year, the social situation of the dental clinical and educational situation is changing.⁵ However, it is difficult for undergraduate dental students to treat many patients during dental clinical training⁶ because patients who receive treatment from them are decreasing and a 1-year internship program is introduced as a matter of duty. Therefore, the methods of dental education are changing and developing at each dental faculty or dental college. The robot patient, which was designed as a full-body model and dental simulation system, was developed³ and introduced to maintain and improve clinical ability. In the present study, undergraduate dental students who finished clinical training during the past year were evaluated for their clinical attitude and ability using a questionnaire survey and accurateness in preparing an abutment using SIMROID as a robot patient and CLINSIM as a traditional

1 mannequin.

2 Consideration of the patients' expressions or attitude was acquired as the main
3 feature of SIMROID,³ while CLINSIM aimed at the improvement of clinical skills such
4 as abutment preparation. Students who experienced dental clinical training and took
5 care of some patients during the past year reported a very close resemblance of the oral
6 condition as their impression of SIMROID because they answered "very same" or
7 "somewhat same" about it after the first and second practical clinical trials. Furthermore,
8 text data mining analysis showed that a "positive" opinion, which was acquired through
9 the sensitivity analysis, was connected with "actual," while "patient" was picked up as
10 frequently appearing words about the expression of SIMROID. These results suggested
11 that undergraduate dental students might be able to practice giving more consideration
12 to patients while seeing the expression of SIMROID in the midst of the same
13 nervousness as treating actual patients.⁴

14 It is an important dental skill to judge and respond to pain or discomfort from a
15 patient's expression or physical condition during dental treatment.⁷ This ability may
16 allow patients to receive dental services safely and comfortably.⁸ However, in the
17 traditional mannequin, it is impossible to manage dental treatment and to practice while
18 seeing the expression or condition of the patient because there is no information from
19 it.⁹ For the results of the consideration or pain during the abutment preparation, because
20 SIMROID had a significantly higher score (2 times) than CLINSIM, it can be a better
21 choice. The consideration for treatment safety during the practical clinical trial had the
22 same results as for physical pain. The role of the simulator reported that clinical training
23 to consider a patient's safety was very important.¹ The results of the investigation
24 suggested that SIMROID was a sufficient educational system to consider pain and

1 treatment safety during practice.^{3,4,10} Tanzawa et al. reported that the robot patient was
2 useful in portraying physical conditions from its facial expressions, physical appearance,
3 and communication for medical emergency education.⁹ The requirements of a dental
4 treatment practice are to evaluate the physical condition as well as the oral condition
5 through a patient's expression or appearance.

6 The recognition of a clean area in medical and dental treatment is a very
7 important conceptual idea and is indispensable because it is not only for the prevention
8 of the spread of infection¹¹ but also for infection control for patients, dentists, and dental
9 co-workers.^{12,13} The knowledge and attitude for infection control had to be required of
10 undergraduate dental students,^{14,15} and naturally, dentists must acquire them.¹⁶ In the
11 present study, the consciousness of maintaining a clean area was 1.2 times higher in the
12 second practical clinical trial than in the first practical clinical trial for SIMROID.
13 Moreover, SIMROID was significantly higher (1.7 times) than CLINSIM. The students
14 could consider the clean area sufficiently and repeated practice was important for
15 infection control awareness.¹³

16 Since abutment preparation requires frequent dental treatment, undergraduate
17 dental students are practicing it in the skills laboratory using the traditional mannequin.
18 In recent years, abutment tooth preparation that dental students fabricate in clinical
19 practice is scanned and evaluated by a 3-dimensional scanning machine using jaw
20 models or traditional mannequins, and that made the evaluation accuracy higher and
21 might enhance learning.¹⁷ The present study examined the difference between
22 SIMROID and CLINSIM for the task-elapsed time and each taper of the abutment
23 preparation on the same tooth.^{18,19} The second practical clinical trial for the task-elapsed
24 time significantly decreased by about 65% compared to the first practical clinical trial.

Moreover, the taper of the bucco-palatal plane significantly decreased the angle in the second practical clinical trial than in the first. However, other tapers did not show a significant difference between the first and second practical clinical trials. Furthermore, the task-elapsed time and the taper showed no significant difference between SIMROID and CLINSIM. These meant that the training systems had little influence on abutment preparation, but the training experience had a tendency to decrease the bucco-palatal taper.²⁰ This result suggested that the training experience and appropriate evaluation led to an improved skill for abutment preparation.¹⁷

The present study has 2 limitations; first, the research covered undergraduate dental students who had just finished their clinical training, but not the dental students before their clinical training. Therefore, because the comparison between before and after clinical training using SIMROID and CLINSIM was not performed for the evaluation of the consideration for the patient, the effect of each system was unclear. However, it was easy to compare SIMROID and CLINSIM with actual patients because the students experienced actual communication and treatment in clinical training similar to that of real patients. This result was based on the free description of the students. Second, the instructor controlled the robot patient's movement through the panel interface on the controller instead of using preprogrammed scenarios in SIMROID.³ The reason for not using a scenario was that the study design gave the situation of SIMRIOD a resemblance to CLINSIM. Therefore, our results suggested that SIMROID was useful in developing the communication and consideration skills for patients and in evaluating treatment attitudes and clinical skills as a practical test.²¹

It was regrettable that the number of students who wanted to take part in this study was small because others did not have any time to participate in the study. Future

1 studies with a large sample size are needed to compare two different groups using SIMROID,
2 CLINSIM, and authentic simulated dental preclinical training to better understand the effectiveness
3 of a humanoid robot patient simulation system

4 The null hypothesis, which stated that SIMROID had the same performance as
5 CLINSIM as a dental education tool, was rejected in this study. It was important to
6 require repeated practice to shorten the task-elapsed time and develop clinical skills.

8 **Conclusions**

9 In recent years, dental students have seen developments in the dental education system
10 to keep pace with the changes in medical and social conditions. They receive instruction
11 using developed robot patients³ as well as computers for education support.^{22,23} This
12 study used a questionnaire survey and an evaluation of abutment tooth preparation by
13 comparing a robot-based interactive patient stimulation system and a traditional
14 mannequin. The results demonstrated that students' attitude significantly improved
15 using the robot patient in comparison with the traditional mannequin. The use of a robot
16 patient system might improve consciousness in giving consideration for the patient
17 during dental treatment.

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Figure Legends

Figure 1-1. Robot-based interactive patient stimulation system (SIMROID)

Figure 1-2. Touch panel control monitor (SIMROID)

Figure 2. The traditional dental training system (CLINSIM)

Figure 3-1. Abutment preparation using SIMROID

Figure 3-2. Abutment preparation using CLINSIM

Figure 4. Schematic representation of the study design showing the practical training and self-report data collection

Figure 5-1. Three-dimensional shape-measuring device

Figure 5-2. Calculation of taper for the abutment preparation model using the 3-dimensional shape-measuring device

Figure 6. Did you feel that the oral cavity of SIMROID was different from that of an actual patient (Q1)?

1) Very different 2) Somewhat different 3) Somewhat same 4) Very same

Participants answered this question for SIMROID after each practical clinical trial.

“Grade” (vertical axis) means the answer in the 4-choice question. “Number”

(horizontal axis) means the number of the students who answered the above question.

Figure 7. Did you feel a level of difficulty to do an abutment preparation using
SIMROID against CLINSIM (Q2)?

1) Very difficult 2) Somewhat difficult 3) Somewhat easy 4) Very easy

Figure 8-1. Are you hopeful of doing the practical training again using each system
(Q3)?

CLINSIM: 1) No hope 2) Very little hope 3) Somewhat hopeful 4) Very
hopeful

SIMROID: 1) No hope 2) Very little hope 3) Somewhat hopeful 4) Very
hopeful

Participants answered this question for each training system after each examination.

“Grade” (vertical axis) means the answer in the 4-choice question. “Number”
(horizontal axis) means the numbers of the participants who answered the above
question. A statistical evaluation was carried out for the comparison between the first
and second examinations and between SIMROID and CLINSIM for each examination.

Figure 8-2. Did you consider the physical pain of the patient (Q4)?

CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often

SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often

Figure 8-3. Did you consider the treatment safety for the patient (Q5)?

CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often

1 SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often

2

3 Figure 8-4. Did you consider the clean area during the practical clinical trial (Q6)?

4 CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often

5 SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often

6

7 Figure 8-5. Were you satisfied with your abutment preparation (Q7)?

8 CLINSIM: 1) Very dissatisfied 2) Somewhat dissatisfied 3) Somewhat satisfied

9 4) Very satisfied

10 SIMROID: 1) Very dissatisfied 2) Somewhat dissatisfied 3) Somewhat satisfied

11 4) Very satisfied

12

13 Figure 9. The high-frequency words were picked up from the free format reports the

14 participants wrote about SIMROID in each practical clinical trial

15

16

17

Table 1. Questions after the first and second practical clinical trials of abutment preparation

1. Did you feel that the oral cavity of SIMROID was different from that of an actual patient?
1) Very different 2) Somewhat different 3) Somewhat same 4) Very same
2. Did you feel a level of difficulty to do an abutment preparation using SIMROID against CLINSIM?
1) Very difficult 2) Somewhat difficult 3) Somewhat easy 4) Very easy
3. Are you hopeful of doing the practical training again using each system?
CLINSIM: 1) No hope 2) Very little hope 3) Somewhat hopeful 4) Very hopeful
SIMROID: 1) No hope 2) Very little hope 3) Somewhat hopeful 4) Very hopeful
4. Did you consider the physical pain of the patient?
CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often
SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often
5. Did you consider the treatment safety for the patient?
CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often
SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often
6. Did you consider the clean area during the practical examination?

CLINSIM: 1) Never 2) Rarely 3) Sometimes 4) Often

SIMROID: 1) Never 2) Rarely 3) Sometimes 4) Often

7. Were you satisfied with your abutment preparation?

CLINSIM: 1) Very dissatisfied 2) Somewhat dissatisfied 3) Somewhat satisfied 4) Very satisfied

SIMROID: 1) Very dissatisfied 2) Somewhat dissatisfied 3) Somewhat satisfied 4) Very satisfied

8. What do you think about the humanoid abilities of showing expression of SIMROID? (Free description)

Table 2. Evaluation of the task-elapsed time and taper between SIMROID and CLINSIM in the first and second practical clinical trials

	SIMROID		CLINSIM		rANOVA		
	First	Second	First	Second	Interaction ^a	Practice ^b	System ^c
Task-elapsed time (sec.)	1619.30 ± 538.21 *	1101.40 ± 394.80 *	1565.00 ± 609.00 **	1011.50 ± 328.97 **	0.86	< 0.01	0.71
Mesio–Distal (degree)	20.42 ± 12.64	21.99 ± 9.25	18.24 ± 10.67	17.87 ± 12.08	0.74	0.84	0.46
Bucco–Palatal (degree)	26.46 ± 8.60	21.82 ± 9.01	29.42 ± 10.58 *	19.55 ± 6.96 *	0.37	0.02	0.90
Corner 1 (degree)	22.32 ± 9.22	19.86 ± 10.48	19.39 ± 14.18	12.32 ± 9.63	0.46	0.14	0.19
Corner 2 (degree)	18.54 (1.40 - 46.96)	21.91 (8.90 - 39.13)	22.89 (10.42 - 51.92)	18.81 (14.03 - 57.80)	0.69	0.75	0.49

Mean ± standard error for variables with normal distribution, median (min-max) for variables with non-normal distribution.

^aThe *P* value of the interaction between practical clinical trial and system with repeated measures ANOVA.

^bThe *P* value between first and second practical clinical trial repeated measures ANOVA.

^cThe *P* value between SIMROID and CLINSIM with repeated measures ANOVA.

Bold characters mean significant difference. "*" or "***" indicate that the *P* value was less than 0.05 for each group.

Corner 1 was the mesio-buccal-disto-palatal corner.

Corner 2 was the disto-buccal-mesio-palatal corner.

Figure 1.1





Figure 1-2

Figure 2



Figure 3-1





Figure 3-2

Figure 4

Group A

CLINSIM



SIMROID



First practical clinical trial: taking a self-report data



SIMROID



CLINSIM



Second practical clinical trial: taking a self-report data

Rest for 30 minutes

*

One month

Rest for 30 minutes

Group B

SIMROID



CLINSIM



First practical clinical trial: taking a self-report data



CLINSIM



SIMROID



Second practical clinical trial: taking a self-report data

Figure 5-1



Figure 5.2



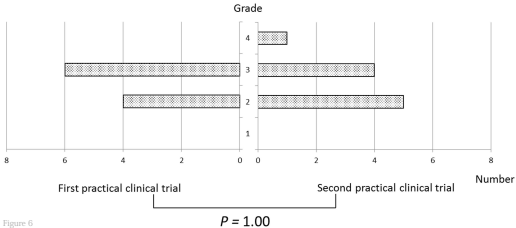


Figure 6

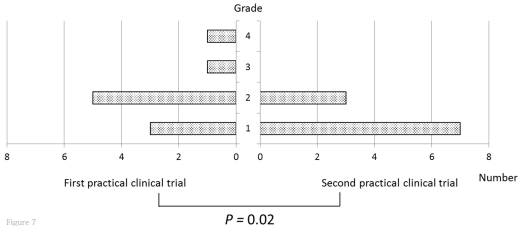


Figure 7

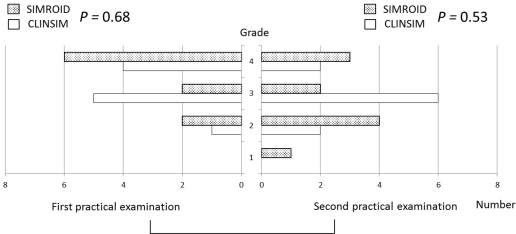


Figure 8-1

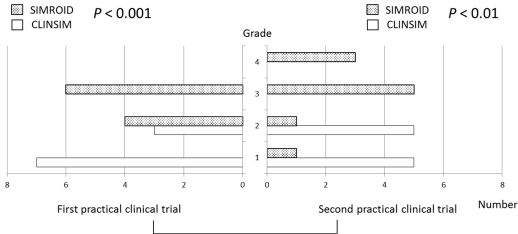


Figure 8-2

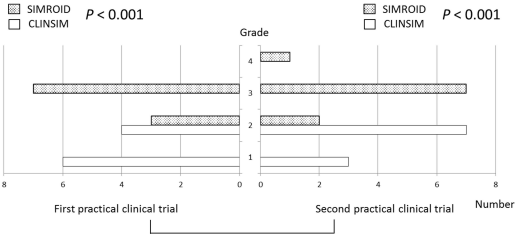


Figure 8-3

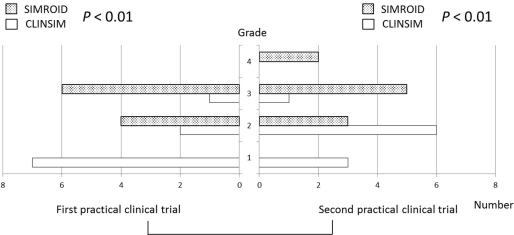
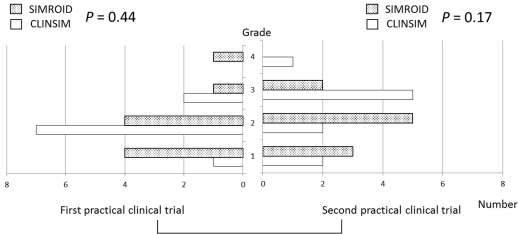


Figure 8-4

First practical clinical trial vs second practical clinical trial (CLINSIM) $P = 0.16$

First practical clinical trial vs second practical clinical trial (SIMROID) $P = 0.08$



First practical clinical trial vs second practical clinical trial (CLINSIM) $P = 0.27$
 First practical clinical trial vs second practical clinical trial (SIMROID) $P = 0.89$

High-frequency words

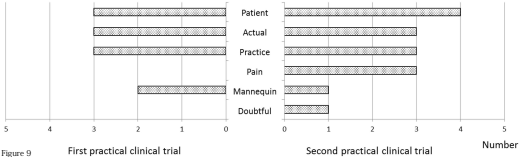


Figure 9